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Risk Factors for Multidrug-Resistant Tuberculosis (MDR-TB) Among Human Immunodeficiency Virus (HIV)-Infected Patients in Northwestern Nigeria

Egbenoma Andrew Aigboeghian[1, *], Simon Ikechukwu Enem[2], Preciousgift Orhue Isibor[3]

[1]Institute of Human Virology Nigeria, Abuja, Nigeria

[2]Department of Veterinary Public Health and Preventive Medicine, Faculty of Veterinary Medicine, University of Abuja, Abuja, Nigeria

[3]Department of Biology, College of Science and Health, William Paterson University of New Jersey, Wayne, USA

Email address:

egbenomaandrew@gmail.com (Egbenoma Andrew Aigboeghian)

[*]Corresponding author

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Abstract: Multidrug-resistant tuberculosis (MDR-TB) is a major threat to tuberculosis (TB) control, and a common occurrence among HIV-infected patients in Nigeria. MDR-TB represents TB simultaneously resistant to at least rifampicin and isoniazid. This study aimed to identify the risk factors for MDR-TB among HIV-infected patients from four Northwestern Nigeria states attending treatment in Aminu Kano Teaching Hospital. A hospital-based retrospective case-control study was conducted by reviewing the clinical records of HIV-infected patients tested for MDR-TB from January 2015 to January 2017. A total of 111 MDR-TB cases were obtained, with equal number (111) of randomly selected controls for this study. We used a descriptive statistical technique to obtain summary values for cases and controls. Variables that showed significant association in bivariate analysis were subjected to multivariable logistic analysis. The independent predictors for MDR-TB were Female Sex (AOR=48.26, 95%, Cl: 6.39-365.88), Rural Residence (AOR=4.09, 95%, Cl: 2.05-8.17) and Age (26-45 years) (AOR=1.34, 95%, Cl: 0.56-3.59). Factors such as; Currently Married, Not Currently Married, Previously Treated and Previously Untreated showed no statistical significance at $p>0.05$. This study identified Female Sex, Rural Residence, and Age (26-45 years) as risk factors for MDR-TB among HIV-infected patients in Northwestern Nigeria. We recommend a prospective study for further understanding of the clinical outcomes of TB treatment and disease.

Keywords: Multidrug-Resistant Tuberculosis (MDR-TB), HIV, Risk Factor, Nigeria

1. Introduction

In sub-Saharan Africa, HIV burden has become a serious challenge, and 30% of active tuberculosis patients are likewise infected with HIV [1, 2]. Multidrug-resistant (MDR) tuberculosis (TB) is TB in patients whose isolated bacilli are resistant in vitro to at least both anti-TB drugs (isoniazid and rifampicin). Recently a meta-analysis has shown that newly infected HIV patients with tuberculosis (TB) co-infection are at more risk of MDR-TB compared with non HIV-infected patients. The risk has not been vividly defined for TB patients with previous treatment history [3, 4]. Although antiretroviral treatment for HIV lessens this risk, TB remains increasingly successive in people living with HIV infection [5]. Moreover, the rates of TB are significantly decreasing in recent years, concurrent spontaneous increase in the relative contribution of MDR-TB and extensively drug resistant tuberculosis (XDR-TB) are alarming [6] and it calls for concern. Consideration has not been given to MDR-TB in sub-Saharan Africa until recently, where significant number of TB occurrence and risk factors were studied. Though much is not known about the risk factors for MDR-TB in Africa, as majority of the studies were drug-resistant studies not risk factor studies. However, being a young male, HIV infection, diabetes mellitus, history of known contact with

TB, use of alcohol, malnutrition, poverty, and patients with anti-TB treatment history were hypothesized as risk factors [7]. A substantial number of patients are receiving treatment outside the direct observed therapy (DOTs) program. These patients may not be treated in accordance with national protocol and consequently inclining such patients to develop resistance tuberculosis [8]. The Nigerian Federal Ministry of Health reveals that 10% of yearly TB cases are re-treatment cases. The distribution of recent and re-treated cases of MDR-TB in Nigeria was revealed to be 1.9% and 9.3% respectively [1]. Some studies have reported 4% and 53% rates of MDR-TB in Abuja and Ibadan respectively [9-11].

Factors associated with the acquisition of MDR-TB may be different among countries and regions, it is therefore imperative to conduct local studies to identify local factors associated with MDR-TB.

This study aimed at determining the independent predictors of MDR-TB among HIV-infected patients. We conducted a retrospective case-control study to assess patients' clinical data between January 2017 to January 2018.

2. Material and Method

2.1. Study Area

The study was carried out at the Regional Tuberculosis Laboratory located in Amino Kano Teaching Hospital, northwestern Nigeria. It covered sampled cases from four randomly selected northwestern Nigeria states; Kano, Katsina, Jigawa and Kebbi. Aminu Kano Teaching Hospital Tuberculosis Laboratory was at this time supported by Global Fund through the Institute of Human Virology Nigeria for tuberculosis diagnosis and treatment monitoring as well as aiding care for all referral susceptible and resistant tuberculosis cases of HIV- infected patients.

2.2. Study Design

A retrospective case-control study was conducted to assess the sociodemographic and treatment-related factors suspected to be associated with MDR-TB among HIV-infected patients between January 2015 to January 2017. MDR-TB test related information were extracted from the data contained in the laboratory record of Amino Kano Teaching Hospital Regional Tuberculosis Laboratory. A random sampling by balloting was applied in the selection of the representative states. The cases and controls were selected from the study population; controls were randomly selected [12]. The variables considered were: age, sex, residence, treatment history and marital status, the level of associations between the independent variables and the disease were determined using odd ratios. Variables that showed statistical significance in the bivariate analysis were subjected to multivariable logistic regression analysis to determine independent determinants of MDR-TB.

2.3. Study Population

The study included all HIV-infected patients from Kano, Katsina, Jigawa and Kebbi tested for MDR-TB in Amino Kano Teaching Hospital between January 2015 to January 2017.

2.4. Case Definition

All HIV-infected patients with sputum smear positive for *Mycobacterium tuberculosis* resistant to at least Isoniazid and Rifampicin as confirmed by molecular line probe assay.

2.5. Selection of Control

All HIV-infected patients confirmed negative for *Mycobacterium tuberculosis* resistant to at least Isoniazid and Rifampicin by molecular line probe assay and Gene Xpert MTB/RIF.

2.6. Inclusion Criteria

All HIV-infected patients with determinate results for the presence or absence of *Mycobacterium tuberculosis* strain resistant to at least Rifampicin and Isoniazid as detected by molecular Line Probe Assay (LPA) from the year January 2015 to January 2017 documented in the clinical laboratory record.

2.7. Exclusion Criteria

All patients with indeterminate result were excluded from the study.

2.8. Sample Size Determination and Sampling

The sample size for cases and controls was calculated using Epi info 6.04 software, Odd ratio of 2.55, a 1:1 ratio between cases and controls, 80% power, and 95% confidence level [13]. However, all the cases found (111 cases) from January 2015 to January 2017 were considered with equal number of controls (111) in this study.

2.9. Data Collection and Analysis

LPA data on identified cases of multidrug-resistant pulmonary tuberculosis were obtained from the data tools of the regional TB laboratory in Amino Kano Teaching Hospital with the assistance of well-trained health workers and laboratory data clerks. All data were correlated with the information contained in the antiretroviral treatment register and the local government TB registers at the patients' care centers. A third party medical data analyst validated the collected data. Data were entered using excel version 2013 and analyzed by Statistical Package for the Social Sciences (SPSS) version 21. A descriptive statistics method was used to obtain values for cases and controls. The strength of association between the independent variables and MDR-TB was determined in a bivariate analysis. At $p<0.05$ statistical significance was established. Variables that showed statistical significance in the bivariate analysis were subjected to multivariable logistic regression analysis to assess independent predictors of MDR-TB.

2.10. Ethical Approval

Ethical clearance was obtained from the Ethical Review

Committee of Aminu Kano Teaching Hospital before the commencement of data collection. Ethical approval number: *NHREC/21/08/2008/AKTH/EC/2183, AKTH/MAC/SUB/12A/P-3/VI/2283*.

3. Result

3.1. Socio-Demographic Characteristics of Cases and Controls

Cases and controls were characterized according to Age, Sex, Marital status and Residence (Table 1). The age group, ≤ 25 years, 26-45 years and >45 years constituted 19.8%, 64.0% and 16.2% of the cases and 39.6%, 49.5% and 10.8% of the controls respectively. Male and Female genders were 59.5% and 40.5% of the cases and 99.1% and 0.9% of the controls respectively. Currently Married and Not Currently Married were 51.4% and 48.6% of the cases and 72.1% and 21.9% of the controls respectively. Urban Residence and Rural Residence were 36.0% and 64.0% of the cases and 78.4% and 21.6% of the controls respectively.

3.2. Bivariate Analysis of MDR-TB Cases and Controls

The age (>45 years) and age (26 – 45 years) showed association with MDR-TB with Crude Odd Ratio (COR) of 1.57 and 1.16 respectively. Female gender showed the highest association with MDR-TB (COR 45) among other variables. Rural residence had COR of 2.96. The currently married and the not currently married had COR of 0.71 and 1.74 respectively but showed no statistical significance at $p > 0.05$.

3.3. Bivariate Analysis of Tuberculosis-Treatment Related Conditions

HIV-infected patients who had no previous TB treatment showed no association with MDR-TB (COR=0.28) while patients previously treated of TB were associated with MDR-TB (COR=1.14). However, this association was not statistically significant at $p>0.05$.

Table 1. *Socio-demographic characteristics of HIV-infected patients with confirmed cases of MDR-TB and those without MDR-TB (selected controls) at Aminu Kano Teaching Hospital Regional Tuberculosis Laboratory Between January 2015 to January 2017.*

S/N	Variables	Case N (%)	Control N (%)
1	Age (years)		
	≤ 25	22 (19.8)	44 (39.6)
	26-45	71 (64.0)	55 (49.5)
	>45	18 (16.2)	12 (10.8)
2	Sex		
	Female	45 (40.5)	1 (0.9)
	Male	66 (59.5)	110 (99.1)
3	Marital Status		
	Currently Married	57 (51.4)	80 (72.1)
	Not Currently Married	54 (48.6)	31 (27.9)
4	Residence		
	Rural	71 (64.0)	24 (21.6)
	Urban	40 (36.0)	87 (78.4)

Table 2. *Bivariate analysis of the socio-demographic characteristics of HIV-infected patients with confirmed cases of MDR-TB and those without MDR-TB (selected controls) tested at Amino Kano Teaching Hospital Regional Tuberculosis Laboratory, Kano State between January 2015-January 2017.*

S/N	Variables	Case N (%)	Control N (%)	COR
1	Age (years)			
	≤ 25	22 (19.8)	44 (39.6)	0.64*
	26-45	71 (64.0)	55 (49.5)	1.16*
	>45	18 (16.2)	12 (10.8)	1.57*
2	Sex			
	Female	45 (40.5)	1 (0.9)	45.0*
	Male	66 (59.5)	110 (99.1)	0.60*
3	Marital Status			
	Currently Married	57 (51.4)	80 (72.1)	0.71**
	Not Currently Married	54 (48.6)	31 (27.9)	1.74**
4	Residence			
	Rural	71 (64.0)	24 (21.6)	2.96*
	Urban	40 (36.0)	87 (78.4)	0.50*

Note: * variables that showed statistical significance during bivariate analysis at $p<0.05$
**Variables that do not show statistical significance at $p>0.05$.

3.4. Multivariable Logistic Analysis for Risk Factors of MDR-TB Among HIV-Infected Patients

The variables found to be independent predictors for MDR-TB among HIV infected patients were Female sex, Age (26-45 years) and Rural Residence (Table 3). HIV-infected females were 48.26 more likely to develop MDR-TB compared to their male counterparts. Patients living in rural areas were 4.09 times more likely to develop MDR-TB compared to patients

living in urban areas. Patients in the age group 26 – 45 years were 1.34 times more likely to develop MDR-TB.

Table 3. *Bivariate analysis of the association of tuberculosis-treatment related conditions with MDR-TB among HIV-infected patients at Amino Kano Teaching Hospital.*

S/N	Variables	Case N (%)	Control N (%)	COR (95% Cl)
1	Treatment history			
	Previously Untreated	5 (4.5)	18 (16.2)	0.28**
	Previously Treated	106 (95.5)	93 (83.8)	1.14**

Note: * variable that showed statistical significance during bivariate analysis at p<0.05,
**Variables that do not showed statistical significance at p>0.05.

Table 4. *Multivariable Logistic Analysis for Risk Factors of MDR-TB among HIV-infected Patients, Aminu Kano Teaching Hospital Regional Tuberculosis Laboratory, Kano.*

S/N	Variables	Case N (%)	P-Value	AOR (95% Cl)
1	SEX			
	Female	46 (20.7)	0.000	48.26 (6.39 – 365.88)
2	RESIDENCE			
	Rural	95 (42.7)	0.000	4.09 (2.05 – 8.17)
3	AGE			
	≤ 25 Years	66 (29.7)	0.029	0.53 (0.18 – 1.58)
	26 – 45 Years	126 (56.8)	0.040	1.34 (0.56 – 3.59)

*Excluded last groups were selected as Reference Category (Male, Urban Residence and Age >45)
Key: COR = Crude Odds Ratio
AOR = Adjusted Odds Ratio.

4. Discussion

In this study, female sex, age (26-45 years), and rural residence were significantly associated with MDR-TB among HIV-infected patients. Workicho et al. in 2017 and Baya et al. in 2019 confirmed age ≤30 years and age ≤40 years respectively to be associated with MDR-TB [14, 15]. The association showed by rural residence (COR 2.96) with MDR-TB could be explained by the socioeconomic vulnerability, poor treatment adherence, and lack of adequate access to proper medical care in rural areas [16]. Previously treated TB patients showed association (COR 1.14) with MDR-TB but this association was not statistically significant at p>0.05. A similar study reported that previously treated TB patients were 21 times more likely to develop MDR-TB compared to those who had no history of previous TB treatment [17]. Female sex (AOR 48.26), rural residence (AOR 4.09), and age (26-45 years) (AOR 1.34) were independent risk factors for MDR-TB. This is consistent with the study conducted in Kazakhstan [18]. We found that HIV-infected females were 48.26 times more likely to develop MDR-TB compared to their male counterparts. A similar study identified the female sex as an independent predictor for MDR-TB among re-treated patients [19]. This could be explained by the fact that religion and cultural restrictions limit northwestern Nigerian women from accessing the expertise of opposite-sex clinicians thereby preventing adequate health information and care. The result of this study showed that rural residents were 4.09 times more likely to develop MDR-TB as compared to urban residents. This could be due to the limited number of well-trained health workers in rural areas, therefore, drive for drug uptake and treatment adherence are lacking. HIV Patients in the age group 26-45 years were 1.34 times more likely to develop MDR-TB compared to the Age group >45 years.

Patients with locally identified risk factors for MDR-TB should be prioritized in local TB programs until findings from any further study are known [20]. This could help curb MDR-TB locally. This study has given a clue that will help in the programmatic implementation of MDR-TB epidemic control among HIV-infected cohorts in northwestern Nigeria.

5. Conclusion

This study has established the sociodemographic predictors of MDR-TB among HIV-infected patients from four (4) Northwestern Nigeria states attending treatment in Aminu Kano Teaching Hospital. Female gender, Rural residence and Age (26-45 years) were independent risk factors associated with MDR-TB among HIV-infected patients. We have provided necessary information for an effective MDR-TB diseases prevention and control programs for HIV-infected patients. We recommend further studies using cross sectional and prospective study-design to understand factors associated with TB incidence and clinical outcomes of TB treatment and disease.

Conflicts of Interest

The authors declare that they have no competing interests.

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References

[1] Sulehri, S. A. (2022). Study on the Bio-physiological and biochemical Assessment of Tuberculosis Patients using Anti TB Drugs in Baluchistan. Pak-Euro Journal of Medical and Life Sciences, 5 (2), 497-500.

[2] Mathias, T., Bright Laban, W., & Patrick, O. (2022). Factors Associated with Treatment Adherence of Patients on Anti-Tuberculosis Drugs Following Covid-19 Pandemic at Health Facilities of Masaka City, Uganda.

[3] Molla, K. A., Reta, M. A., & Ayene, Y. Y. (2022). Prevalence of multidrug-resistant tuberculosis in East Africa: A systematic review and meta-analysis. Plos one, 17 (6), e0270272.

[4] Muntean, A. C. (2022). Case Report: Pulmonary Tuberculosis Reactivation in Patients with Human Im-munodeficiency Virus: A Case Report. Ann Clin Med Case Rep, 9 (7), 1-3.

[5] Wallis, R. S., O'Garra, A., Sher, A., & Wack, A. (2022). Host-directed immunotherapy of viral and bacterial infections: past, present and future. Nature Reviews Immunology, 1-13.

[6] Seo, H., Kim, S., Mahmud, H. A., Islam, M. I., Yoon, Y., Cho, H. D. & Song, H. Y. (2022). A novel class of antimicrobial drugs selectively targets a Mycobacterium tuberculosis PE-PGRS protein. PLoS Biology, 20 (5), e3001648.

[7] Xi, Y., Zhang, W., Qiao, R. J., & Tang, J. (2022). Risk factors for multidrug-resistant tuberculosis: A worldwide systematic review and meta-analysis. PloS one, 17 (6), e0270003.

[8] Salami, A. K., & Oluboyo, P. O. (2003). Management outcome of pulmonary tuberculosis: a nine-year review in Ilorin. West African journal of medicine, 22 (2), 114-119.

[9] Otokunefor, K., Otokunefor, T. V., & Omakwele, G. (2018). Multi-drug resistant Mycobacterium tuberculosis in port harcourt, Nigeria. African Journal of Laboratory Medicine, 7 (2), 1-4.

[10] George, O. T., & Oduyebo, O. O. (2022). Detection of multi-drug resistant tuberculosis (MDR TB) using microscopic observation drug susceptibility (MODS) assay in Lagos State, southwest Nigeria. African Journal of Clinical and Experimental Microbiology, 23 (2), 174-181.

[11] Sebastião, C. S., Samulengo, J., Sacomboio, E., Francisco, N. M., Teixeira, C., António, S.,... & Morais, J. (2022). Epidemiological Characteristics and Risk Factors Related to Drug-resistant Tuberculosis in Luanda, Angola. The American Journal of Tropical Medicine and Hygiene, 1 (aop).

[12] Fikre, A., Tewelde, T., & Shaweno, T. (2019). Determinants of multi-drug resistant tuberculosis among tuberculosis patients in Southern Ethiopia: a case control study. Journal of Medical Bacteriology, 8 (1-2), 1-12.

[13] Mulu, W., Mekkonnen, D., Yimer, M., Admassu, A., & Abera, B. (2015). Risk factors for multidrug resistant tuberculosis patients in Amhara National Regional State. African health sciences, 15 (2), 368-377.

[14] Workicho, A., Kassahun, W., & Alemseged, F. (2017). Risk factors for multidrug-resistant tuberculosis among tuberculosis patients: a case-control study. Infection and drug resistance, 10, 91.

[15] Baya, B., Achenbach, C. J., Kone, B., Toloba, Y., Dabitao, D. K., Diarra, B. & Diallo, S. (2019). Clinical risk factors associated with multidrug-resistant tuberculosis (MDR-TB) in Mali. International Journal of Infectious Diseases, 81, 149-155.

[16] Suchindran, S., Brouwer, E. S., & Van Rie, A. (2009). Is HIV infection a risk factor for multi-drug resistant tuberculosis? A systematic review. PloS one, 4 (5), e5561.

[17] Tenzin, C., Chansatitporn, N., Dendup, T., Dorji, T., Lhazeen, K., Tshering, D., & Pelzang, T. (2020). Factors associated with multidrug-resistant tuberculosis (MDR-TB) in Bhutan: A nationwide case-control study. Plos one, 15 (7), e0236250.

[18] World Health Organization. (2016). Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations.

[19] Lomtadze, N., Aspindzelashvili, R., Janjgava, M., Mirtskhulava, V., Wright, A., Blumberg, H. M., & Salakaia, A. (2009). Prevalence and risk factors for multidrug-resistant tuberculosis in the Republic of Georgia: a population-based study. The International journal of tuberculosis and lung disease, 13 (1), 68-73.

[20] Mulisa, G., Workneh, T., Hordofa, N., Suaudi, M., Abebe, G., Jarso, G. (2015). Multidrug-resistant Mycobacterium tuberculosis and associated risk factors in Oromia Region of Ethiopia. Int. J. Infect. Dis. 39, 57–61.